THE **TRIAL** BLAZER

UPMC HILLMAN CANCER CENTER

A quarterly newsletter from CLINICAL RESEARCH SERVICES

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INTRODUCTION

Update on CCSG Core Grant

As you are all aware, we are preparing our renewal application for the NCI Comprehensive Cancer Center Support Grant (CCSG) for submission in late September. Providing access to state-of-the-art clinical trials to cancer patients in the catchment area is one of the most important evaluation criteria in the CCSG application. We are the only NCI-designated Comprehensive Cancer Center in western Pennsylvania, and UPMC's world-class clinical care and research excellence sets us apart from the competition. With strong support from the Hillman faculty and oncologists in the Hillman network, we have treated 500 patients on therapeutic clinical trials in the first half of 2019, a 22 percent increase from last year, and enrolled 691 patients on interventional trials (including therapeutic). This increase is a testament to the commitment and hard work of all our physicians as well as clinical and CRS staff.

We are opening several exciting cutting-edge trials, described in this newsletter. With your support, we hope to continue the momentum and surpass 1,000 therapeutic and 1,500 interventional accruals by the end of this year, leading into the site visit by the NCI reviewers in early 2020. We are also preparing for the second annual clinical trial retreat in October, to continue the collaboration between academic and network oncologists. A new Hillman clinical trials app has been designed with input from network oncologists and patients. It is undergoing final beta testing and will be launched in the next few weeks. We hope to gather feedback about the app during the retreat.

Thank you again for your continued support and hard work.

Antoinette (Toni) Wozniak, MD, FACP, FASCO
Associate Director of Clinical Research

Bhanu P. Pappu, PhD, MHA
Vice President of Clinical Operations and Strategy

NEW UNIVERSAL CONSENT FOR GENOMIC SEQUENCING FOR UPMC HILLMAN CANCER CENTER

Do you order genomic testing through Foundation Medicine, TEMPUS, CARIS, or internally through Pathology or the UPMC Genome Center?

As part of our NCI mandate, we have started a new initiative to enroll every patient undergoing SOC/research genomic testing under the new HCC 18-177 protocol that allows our investigators to follow these patients for clinical progression, treatment decisions, and outcomes analysis.

You also have the option to obtain biological specimens for other biomarker analyses. By integrating various data analytics platforms across the cancer center, our goal is to make this new resource available to all Hillman investigators to advance our clinical and research mission.

Please contact any CRS coordinator to enroll your oncology patients who have already had or are going to get genomic testing (retrospective and prospective). The 18-177 protocol is available through this link: 18-177.

This is a joint effort of all HCC investigators, under my direction, in preparation for the CCSG core grant renewal, to guide and improve oncology treatment practices and contribute to advancing preclinical and clinical cancer research at UPMC and the University of Pittsburgh.

Please use 18-177 for all genomic analyses.

Sincerely,

Robert L. Ferris, MD, PhD
Director

POINTS OF INTEREST

Accrual Statistics for 2019

- Open to Accrual (OTA) Studies
- Non-therapeutic (Interventional) Referrals
- Therapeutic Referrals

Priority Trials in the Community

- Breast Cancer
  - > Metastatic Breast Cancer
  - > HER2 Negative Breast Cancer
  - > Triple Negative Breast Cancer
- GI/esophageal
- Pancreatic Cancer
- Lung Cancer

Spotlight Trials

- UPMC Hillman Cancer Center SEQ
- Immunotherapy for HER2-Positive Metastatic Breast Cancer
- Advance Care Planning For Patients with Advanced Cancer and Their Caregivers
- Hematological Malignancies - Therapies for Multiple Myeloma

2019 OPEN STUDIES AND ACCRUALS

Disease and Modality Center	Current Interventional OTA Trials	Current Therapeutic OTA Trials	Interventional Accruals	Therapeutic Accruals
Breast Center	29	24	89	82
GI/Esophageal Cancer Center	11	11	58	58
Melanoma Center	18	18	59	59
Lung and Thoracic Malignancies Center	25	23	66	42
Head and Neck Center	17	17	50	47
Prostate and Urologic Cancers	18	18	44	44
Hematological Malignancies Center	33	33	36	27
Phase I Center	25	25	27	27
Pediatric Oncology	48	47	25	25
Brain Tumor Center	9	9	25	25
Gynecological Oncology Center	9	9	21	21
Sarcoma Center	7	7	14	14
Immune Therapy Center	4	4	7	7
Biobehavioral Medicine in Oncology Program	10	0	152	0
Total	**263**	**245**	**673**	**478**
*Radiation Oncology Center	20	20	38	38
*Phase II Center	31	31	22	22

All accruals have been calculated through the 2nd Quarter of 2019 (Jan-Jun).
*Accruals counted within Disease Center of care.

2019 INTERVENTIONAL (NON-THERAPEUTIC) REFERRALS

Referring Physician	Number of Referrals
David Wilson	25
Vincent Reyes	16
John Waas	12
Alexis Megaludis	10
Gauri Kiefer	9
Franklin Viverette	9
Terry Evans	8
Afaq Ahmad	7
William Ferri	7
Amanda Laubenthal	6
Matthew Sulecki	5
Nitin Kapoor	4
Hyoung Kim	4
Christopher Marsh	4

Referrals are as of 06-30-2019

2019 THERAPEUTIC REFERRALS

Referring Physician	Number of Referrals
James Ohr	16
John Kirkwood	13
John Rhee	12
Diwakar Davar	10
Dan Zandberg	10
Vincent Reyes	9
Anastasios Raptis	8
Vikram Gorantla	7
Umamaheswar Duvvuri	6
Terry Evans	6
Frank Lieberman	6
Kit Lu	6
Robert Vanderweele	6

Referrals are as of 06-30-2019

HIGH PRIORITY TRIALS IN THE COMMUNITY

Breast Cancer

Metastatic Breast Cancer

For additional inclusion criteria and information, please contact the respective PIs.

HCC 19-005 : A Phase II Trial of HKI-272 (Neratinib), Neratinib and Capecitabine, and Neratinib and Ado-Trastuzumab Emtansine (T-DM1) for Patients with Human Epidermal Growth Factor Receptor 2 (HER2)-Positive Breast cancer and Brain Metastases

PI: Dr. Adam Brufsky, brufskyam@upmc.edu

This is a very high priority, multi-cohort, phase II, open-label, single arm study with administration of neratinib-based treatments for patients with HER2-positive breast cancer with brain metastases. The study consists of Cohort 1 (progressive brain metastases), 2 (craniotomy candidates), 3A (no prior lapatinib), 3B (prior lapatinib), 4A and B (untreated and treated CNS disease, respectively, both without prior ado-trastuzumab emtansine exposure [T-DM1]), and 4C (progressive CNS disease with T-DM1 exposure). Our primary objective is to evaluate the CNS objective response rate (ORR) CNS response in at least 5 of 40 patients would be considered indicative of the drug's potential for further study.

HCC 13-164: A Trial of Endocrine Response in Women with Invasive Lobular Breast Cancer (ILC)

PI: Dr. Priscilla McAuliffe, mcauliffepf@upmc.edu

This trial aims to determine the change from baseline to post-treatment values of the proliferation marker Ki67 in hormone receptor (HR)-positive, HER2-negative, lobular breast cancer (ILC) tissue derived from postmenopausal women awaiting definitive surgery or further neoadjuvant treatment. Eligible patients will be randomized to receive neoadjuvant endocrine treatments with fulvestrant, anastrozole, or tamoxifen. Our trial will hopefully provide clinical evidence to support the differential treatment of patients with ILC tumors as opposed to other HR-positive breast cancers.

HCC 17-203: Randomized Phase II Study of Pembrolizumab, an anti-PD (programmed cell death)-1 Antibody, in Combination with Carboplatin Compared to Carboplatin Alone in Breast Cancer Patients with Chest Wall Disease

PI: Dr. Leisha Emens, emensla@upmc.edu

The primary objective of this trial is to compare disease control rates at 18 weeks of treatment with pembrolizumab and carboplatin in breast cancer patients with chest wall disease that is hormone resistant (ER positive/PR positive/HER2 negative breast cancer with progressive disease on two prior lines of hormonal therapy) or triple negative (ER negative/PR negative/HER2 negative, TNBC) as well as patients with HER2+ disease whose chest wall disease has progressed on all approved/feasible HER2 targeted therapies. Overall, this study promises to improve our understanding of pembrolizumab for the treatment of breast cancer with chest wall disease.

HCC 18-059: A Phase II Study of Olaparib Monotherapy in Metastatic Breast Cancer Patients with Germline or Somatic Mutations in DNA Repair Genes "Olaparib Expanded"

PI: Dr. Adam Brufsky, brufskyam@upmc.edu

This trial seeks to evaluate the efficacy of monotherapy with the PARP inhibitor, olaparib, in two parallel cohorts of patients with metastatic breast cancer. Cohort 1 consists of patients with germline mutations in DNA repair genes other than BRCA1/2, while patients in Cohort 2 have somatic mutations in DNA repair genes (somatic pathogenic BRCA1 or BRCA2 mutations are permitted in patients who lack a germline mutation in BRCA1 or BRCA2). Positive findings of this trial will support further study of PARP inhibitors in this patient population, with the potential to provide future relatively non-toxic oral therapeutic options to conventional cytotoxic chemotherapy.

HCC 16-015: Treatment of Metastatic BC with Fulvestrant plus Palbociclib or Tamoxifen plus Palbociclib: A Randomized Phase II Trial with ESR1 Mutation in Circulating Tumor DNA (2nd, 3rd line)

PI: Dr. Adam Brufsky, brufskyam@upmc.edu

The primary objective of this study is to compare progression-free survival (PFS) in fulvestrant plus palbociclib and tamoxifen plus palbociclib arms in patients. We will compare patients both unselected by ESR1 mutation and in the subset of patients with ESR1-mt tumors assessed primarily from ctDNA at enrollment. Prospective patients are required to meet the following main inclusion criteria:

- Must have previously received an aromatase inhibitor and palbociclib in the adjuvant, neo-adjuvant, or metastatic setting.
- No more than three lines endocrine therapy and one line chemotherapy in the metastatic setting.

HER2 Negative Breast Cancer

HCC 17-190: A Multinational, Multicenter, Randomized, Phase III Study of Tesetaxel plus a Reduced Dose of Capecitabine versus Capecitabine Alone in Patients with HER2 Negative, Hormone Receptor Positive, Locally Advanced or Metastatic Breast Cancer Previously Treated with a Taxane

Sponsor: Odonate Therapeutics, Inc.

Triple Negative Breast Cancer

HCC 17-160: An International, Multi-Center, Open-Label, Randomized, Phase III Trial of Sacituzumab Govitecan versus Treatment of Physician Choice in Patients with Metastatic Triple-Negative Breast Cancer Who Received at Least Two Prior Treatments

Sponsor: Immunomedics, Inc.

GI/Esophageal Cancer

HCC 17-202: Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) Study: A Randomized Phase III Study of mFOLFOX6/Bevacizumab Combination Chemotherapy with or without Atezolizumab or Atezolizumab Monotherapy in the First-Line Treatment of Patients with Deficient DNA Mismatch Repair (dMMR) Metastatic Colorectal Cancer

PI: James J. Lee, MD, PhD, leejj@upmc.edu

HCC 17-216: A Phase II Study to Assess the Activity of PD-L1 Inhibition with Durvalumab (MEDI4736) after Chemo-Radiotherapy in Patients with Stage II-IV Microsatellite Stable (MSS) Rectal Cancer

Protocol Chair: Thomas George, MD

Pancreatic Cancer

HCC 17-134: Randomized Phase II Trial of Pre-Operative Gemcitabine, Nab-Paclitaxel, and Hydroxychloroquine with or without Avelumab (PGHA vs. PGH)

PI: Dr. Nathan Bahary, baharyn@upmc.edu

Lung Cancer

HCC 14-166: Adjuvant Lung Cancer Enrichment Marker Identification and Sequencing Trial (ALCHEMIST)

Study Chair: Geoffrey Oxnard, MD

HCC 16-153: A Phase II Clinical Trial Evaluating the Efficacy of Atezolizumab in Advanced Non-Small Cell Lung Cancer (NSCLC) Patients Previously Treated with PD-1-Directed Therapy

PI: Dr. Liza Villaruz, villaruzl@upmc.edu

Physicians should contact the study's PI or Donna Haney (Community Network Program Manager, haneydl@upmc.edu) with inquiries.

SPOTLIGHT TRIALS

IMMUNOTHERAPY FOR HER2-POSITIVE METASTATIC BREAST CANCER

HCC 19-041: A Randomized, Double-Blind, Phase III Trial of Paclitaxel/Trastuzumab/Pertuzumab with Atezolizumab or Placebo in First-Line HER2-Positive Metastatic Breast Cancer

PI: Dr. Adam Brufsky, brufskyam@upmc.edu

The primary aim of this trial is to determine whether the addition of atezolizumab to a regimen of paclitaxel, pertuzumab, and trastuzumab will improve the progression-free survival (PFS), assessed using RECIST 1.1 criteria, relative to a paclitaxel, pertuzumab, trastuzumab, and placebo regimen in patients with newly documented HER2-positive measurable metastatic breast cancer. Prospective patients are expected to meet the following, among other, main inclusion criteria:

- De novo metastatic disease presenting without prior history of HER2-positive breast cancer: Diagnosis should have been made from a biopsy of a metastatic disease site, but biopsy from the breast primary or involved regional lymph nodes is acceptable if biopsy of the metastatic sites was thought to carry excessive risk for the patient.
- Locally recurrent or metastatic disease following prior therapy for early breast cancer: Diagnosis must have been made from the biopsy of the locally recurrent or metastatic disease. There must be an interval of ≥ 6 months between completion of neoadjuvant/adjuvant HER2-targeted therapy and documentation of locally recurrent or metastatic HER2-positive disease by biopsy.

Interested physicians can contact the PI or Brenda Lee Steele, Clinical Research Manager-Women's Cancer Research Program, at steeleb@upmc.edu.

IIT – ADVANCE CARE PLANNING FOR PATIENTS WITH ADVANCED CANCER AND THEIR CAREGIVERS

PEACe-compare Trial Comparing the Effectiveness of Two Approaches to Advance Care Planning for Patients with Advanced Cancer and Their Caregivers

PI: Dr. Yael Schenker, yas28@pitt.edu

Yael Schenker, MD, MAS, has received an R01 from the National Cancer Institute to compare the effectiveness of two approaches to advance care planning for patients with advanced cancer and their caregivers. PEACe-compare will enroll 400 patients and their caregivers to receive either an in-person advance care planning visit with a trained facilitator or web-based advance care planning using interactive videos. During the five-year award, this study will provide new and much needed evidence about the most effective and efficient approach to advance care planning in oncology.

For more information, please contact the PI.

HEMATOLOGICAL MALIGNANCIES

THERAPIES FOR MULTIPLE MYELOMA

HCC 19-055: A Randomized Study of Daratumumab plus Lenalidomide vs. Lenalidomide Alone as Maintenance Treatment in Patients with Newly Diagnosed Multiple Myeloma Who Are Minimal Residual Disease Positive after Frontline Autologous Stem Cell Transplant

PI: Dr. Anastasios Raptis, raptisa2@upmc.edu

The purpose of this study is to evaluate conversion rate to minimal residual disease (MRD) negativity, following the addition of daratumumab to lenalidomide relative to lenalidomide alone. This treatment will be administered as maintenance treatment to anti-CD38 treatment-naive participants with newly diagnosed multiple myeloma who are MRD-positive following high-dose therapy (HDT) and autologous stem cell transplant (ASCT), with or without consolidation therapy. Patients should be referred if they are between 18 to 79 years of age, have newly diagnosed multiple myeloma with a history of 4 to 8 total cycles of induction with or without consolidation therapy and have received HDT and ASCT, and show very good partial response or better assessed per the International Myeloma Working Group (IMWG) 2016 criteria at the time of randomization.

Physicians interested in additional information or having their patients screened can contact the PI or Linda Fukas, Clinical Research Supervisor at fukaslj@upmc.edu.

HCC 19-012: A Single Arm, Open-label, Phase II Study of Melflufen in Combination with Dexamethasone in Patients with Relapsed Refractory Multiple Myeloma who are Refractory to Pomalidomide and/or anti-CD38 Monoclonal Antibody

PI: Dr. Anastasios Raptis, raptisa2@upmc.edu

Melflufen is an alkylating peptide, belonging to the novel class of peptidase-enhanced compounds (PEnCs), and targets the MM transformation process with a unique mechanism of action that overcomes resistance pathways of existing myeloma treatments (including alkylators) and demonstrates strong anti-angiogenic properties. Patients should be referred to this study if they are ≥ 18 years old with prior diagnosis of multiple myeloma with documented disease progression in need of treatment at time of screening, have had a minimum of two prior lines of therapy including an IMiD and a PI and are refractory to pomalidomide and/or an anti-CD38 mAb, have a life expectancy ≥ 6 months, and ECOG performance status ≤ 2.

Physicians who are interested in more information and would like to have their patient screened, should please contact the PI or Linda Fukas, Clinical Research Supervisor, at fukaslj@upmc.edu having their patients screened can contact the PI or Linda Fukas, Clinical Research Supervisor at fukaslj@upmc.edu.

HCC 19-029: A Phase IB-II, Open-Label Study of JNJ-68284528, a Chimeric Antigen Receptor T cell (CAR-T) Therapy Directed Against BCMA in Subjects with Relapsed or Refractory Multiple Myeloma

PI: Dr. Mounzer Agha, aghame@upmc.edu

This trial offers patients with multiple myeloma who have exhausted all meaningful standard therapeutic modalities another potentially effective treatment option. Patients must have failed three prior lines of myeloma therapy (that must include PI, and IMiD and an anti-CD38 antibody), or are double refractory to an IMiD and proteasome inhibitor. Patients must have undergone at least one complete cycle of treatment for each regimen.

Patients should be referred to this study, before their disease accelerate rapidly, as there will be an interval of about 4 weeks from lymphocytes apheresis to the CART infusion. Patients must meet eligibility criteria, and one of the most important is serum creatinine clearance of > 40, which is another reason, to enroll patients early before their renal function is compromised by the myeloma.

For more information and to have your patient screened, please contact the PI or Linda Fukas, Clinical Research Supervisor at fukaslj@upmc.edu.

Clinical Research Services (CRS) is made up of over 185 staff members who facilitate development, implementation, coordination, internal data monitoring, and completion of approximately 341 oncology-focused trials at Hillman each year. These trials include institutional (investigator-initiated), multi-center cooperative group/National Clinical Trial Network (NCTN), consortium, and industry-sponsored trials. Using a disease-specific centers model for conducting clinical trials, CRS provides study development and implementation assistance, submissions to the FDA, IRB processing, patient recruitment, study coordination, study-specific training, data collection, and specimen collection and processing.

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